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# Understanding the patterns and distribution of opioid analgesic dependence symptoms using a latent empirical approach

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**Abstract**

*Prevalence of extramedical opioid analgesic use in the US is rising, yet little is known about the nature and extent of problems of dependence related to the use of these drugs. This study uses Latent Class Analysis to empirically define classes of past-year extramedical opioid analgesic users based on observed clustering of DSM-IV defined clinical dependence features; multinomial logistic regression is used to describe differences across these groups. The 2002–2003 public data-files of the National Survey on Drug Use and Health were used to identify 7810 extramedical opioid analgesic users in the past-year. The best-fitting four-class model identified classes that differed quantitatively and qualitatively, with 2% of the users in Class 4 (most severe) and 84% in Class 1 (least severe). Classes 2 and 3 had parallel symptom profiles, but those in Class 3 reported additional problems. Adolescents (12–17 year olds) were at higher odds of being in Class 3 versus older age groups; females were two times as likely to be in Classes 2 and 4, and those with mental health problems were at higher odds of belonging to the more severe classes. Differences by type of past year opioid users were also detected. This study sheds light on the classification and distribution of extramedical opioid analgesic dependence symptoms in the US general population, identifying subgroups that warrant immediate attention. Copyright © 2008 John Wiley & Sons, Ltd.*

**Key words**: opioid analgesics, extramedical use, dependence, epidemiology, Latent Class Analysis

## Introduction

According to the 2005 National Survey on Drug Use and Health (NSDUH), 13.4% of the US population aged 12 years of age or older reported ever using opioid analgesics for non-medical purposes, a prevalence that has been on the rise over the past few years (9.8% in 2001 and 5.8% in 1998) (SAMHSA, 2006). In addition, 2.2 million individuals used these substances for the first time during 2005, and although the number is similar to the corresponding estimates for 2000–2003, it points to a substantial increase since 1990 (627,000 initiates) (SAMHSA, 2006). In 2005, an estimated 1.5 million Americans aged 12 years or older met criteria for extramedical opioid analgesics abuse and/or dependence as per the Diagnostic Statistical Manual, fourth version (DSM-IV) (APA, 1994), representing 12.3% of persons who had used opioid analgesics extramedically during the preceding year (SAMHSA, 2005).

Despite the increasing concern about the recent rise in the extramedical use of opioid analgesics, only a few studies have investigated problems associated with their use (e.g. dependence symptoms) (Huang et al., 2006; Martins et al., 2007; Simoni-Wastila et al., 2004). Many of the concerns about the current 'epidemic' and its associated problems are founded largely on anecdotal and clinical reports (Sproule et al., 1999; Zacny et al., 2003). Other issues with the available data are the idiosyncratic definitions used, and the need for clearer

definitions of misuse, abuse, dependence and/or addiction (Compton and Volkow, 2006).

According to the DSM-IV, substance dependence is defined as a cluster of three or more of the seven dependence symptoms occurring at any time in the same 12-month period. Dependence symptoms are the same for all psychoactive substances (APA, 1994), despite the fact that certain symptoms are less salient for some substances than others, and in a few instances not all symptoms apply. For example, withdrawal symptoms are not specified for hallucinogen dependence in the DSM-IV, despite recent evidence for a hallucinogen dependence syndrome (Stone et al., 2006), which has been shown using Latent Class Analysis (LCA). Even the degree to which tolerance develops varies greatly across substances (APA, 1994). While most individuals with opioid analgesic dependence have significant levels of tolerance and will experience withdrawal on abrupt discontinuation of opioids substances (APA, 1994), tolerance and withdrawal are neither necessary nor sufficient for a diagnosis of opioid analgesic dependence according to the DSM-IV criteria (APA, 1994), the most commonly applied categorical taxonomic system for psychiatric disorders. Reliance on a common categorical approach for assessing dependence across different substances might result in a loss of information regarding heterogeneity in response to drug taking. Further, it is possible that categories of drug dependence problems exist that might be more clinically relevant than those identified using DSM-IV criteria.

LCA empirically classifies observations into distinct groups or classes based on the probability of particular patterns of responses (McCutcheon, 1987). It does not make any assumptions about the presence or absence of opioid analgesic dependence as per traditional diagnostic criteria (i.e. DSM-IV) (APA, 1994). LCA allows for the identification of groups of users based on the associations among a set of symptoms or behaviors they have reported, and not on a cut-off score of three or more of the seven substance dependence criteria (APA, 1994). Thus, the groups may be quantitatively (i.e. gradient in the number of symptoms) or qualitatively different (i.e. classes characterized by a different set of symptoms), which could be highly informative given that the number and pattern of symptoms endorsed may vary by substance (APA, 1994). While not previously applied among opioid analgesic users, Lynskey et al. (2005) used this technique to examine the limitations of DSM-IV operationalizations of alcohol abuse and dependence in a sample of Australian twins and concluded that the conceptualization and measurement of alcohol abuse may need to be refined for women. Similarly, Storr et al. (2005) found that while the vast majority of tobacco smokers were classified congruently using LCA and the Fagerstrom test for nicotine dependence, LCA further provided insight into possible phenotypic differences among tobacco smokers and classified smokers into a higher level of dependence.

Given the lack of research on the nature and extent of problems related to the extramedical use of analgesics, the aims of this study are primarily exploratory and descriptive, and include: (1) empirically identifying groups of extramedical opioid analgesic users using LCA; (2) exploring how certain respondent characteristics, including demographics, use of other drugs and psychiatric comorbidity, are related to group membership as defined by the patterns of responses to the dependence symptoms; and (3) comparing the latent class classification to DSM-IV diagnosis of opioid analgesic dependence in an attempt to increase our understanding of the diagnosis of opioid analgesic dependence.

## Methods

### *Study participants*

The analyses are based on data from the 2002–2003 NSDUH public use data-files (formerly known as the National Household Survey on Drug Abuse; SAMHSA, 2003, 2004). The NSDUH, which is sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA), is a nationally representative multi-stage cluster sampling of household populations aged 12 years or older. In 2002–2003, certain subpopulations (e.g. youths and young adults) were over-sampled. All analyses accounted for the over-sampling and the complexity of the survey design.

The aggregate sample size for 2002–2003 was 109,309. Analyses in this report focused on respondents who reported using opioid analgesics extramedically in the year preceding the survey (i.e. past-year users), given that clinical features of opioid analgesic dependence were only measured among this subgroup ($N$ = 7810). The 'Serious Mental Illness' (SMI) indicator was only assessed among adults (see the section titled 'Assessment and measures'). A separate set of analyses



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incorporating the SMI measure was thus conducted among adults only, aged 18 years or older ($N = 5386$).

Overall response rate was 91% for household screening for both 2002 and 2003, and 79% and 71% for completed interviews in 2002 and 2003, respectively (SAMHSA, 2003, 2004). Detailed information about the sampling and survey methodology in the NSDUH can be found elsewhere (SAMHSA, 2003, 2004).

*Assessment and measures*

The 2002–2003 surveys were administered via computer-assisted instruments. Also, starting in 2002, respondents were offered a $30 incentive payment for their participation, and quality control procedures for data collection were enhanced beginning 2001, setting the data from the 2002 NSDUH as a new baseline for substance use measures (SAMHSA, 2003).

Information on substance use and demographic data was available for all respondents. Demographic variables selected for this study were age, sex, race/ethnicity (White, African-American, Hispanics and other), income and education included as proxy measures for socio-economic status of the respondents.

Questions inquiring about extramedical opioid analgesic use began with a stem question that asked the respondent if s/he had ever used [. . .] more than was described, or without prescription to get high (SAMHSA, 2003, 2004). Symptoms of opioid analgesic dependence included in the survey were operationalized according to the DSM-IV criteria for substance dependence; 10 questions were used to measure the seven symptoms of dependence on all opioid analgesic medications experienced during the 12 months prior to the interview (Table 1).

Past-year opioid analgesic users were categorized into three distinct groups based on their past-year pattern of use of other substances: (1) past-year users of opioid analgesics only (abbreviated as Group A from here on); (2) past-year users of opioid analgesics who were also past-year users of other prescription drugs such as stimulants, sedatives and tranquilizers in the past year (Group AP); (3) past-year users of opioid analgesics who were also past-year users of other prescription drugs, as well as cocaine and/or heroin (Group APCH). We hypothesized that while some individuals may have only used opioid analgesics in the past year, others may have used both opioid analgesics and other prescription drugs non-medically, and some others may have used opioid analgesics, other prescription drugs, and at least one illegal substance (i.e. cocaine and/or heroin). It is important to distinguish Group AP from APCH given other findings that have shown that misuse of opioid analgesics and other prescription drugs (tranquilizers, stimulants, sedatives) often co-occurs among individuals who do not use illegal drugs such as cocaine and heroin (McCabe et al., 2005). Furthermore, our decision to focus only on cocaine and/or heroin, instead of on the use of other legal and illegal substances, stems mainly from the fact that the majority of the past-year opioid analgesic users had in fact used alcohol (86.9%), and a substantial percentage had used marijuana (52.6%) once or more in the preceding year. Previous and current alcohol and other drug use in this sample of opioid analgesic users are more extensively described in a separate paper (Martins et al., 2007).

The SMI indicator included in the NSDUH was used to assess mental health differences across the empirically-derived groups of opioid analgesic users. The SMI is defined using a series of six questions inquiring about the frequency of symptoms of psychological distress during the one month in the past year when respondents felt at their worst emotionally. The symptoms of distress include: feeling nervous, feeling hopeless, feeling restless or fidgety, feeling so sad or depressed that nothing could cheer you up, feeling everything was an effort and feeling no good or worthless. These questions were only administered to adults, aged 18 years and older, using a modified version of the World Health Organization's Composite International Diagnostic Interview Short Form (Kessler et al., 2003). A cumulative score of greater than 13 (on a scale of 0–24) classified the respondent as most likely having a serious mental health problem; a more detailed description of the indicator has been published elsewhere (SAMHSA, 2003, 2004).

*Statistical analyses*

To derive empirically-defined subgroups of opioid analgesic users based on observed clustering of the DSM-IV symptoms of opioid analgesic dependence, LCA was applied using the Latent Gold software (Vermunt and Magidson, 2000). Two weighted models were fit separately for the total sample ($N = 7810$) and adults sample ($N = 5386$) of past year opioid analgesic users. The best-fitting models in each were chosen based on the Bayesian Information Criteria (BIC); the model with the lowest BIC value (i.e. better fit) was selected (Magidson and Vermunt, 2004). Two sets of parameters



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**Table 1.** DSM-IV criteria for substance dependence and corresponding NSDUH items: weighted prevalence in the total and adult sample of extramedical opioid analgesic users, NSDUH 2002–2003

| DSM-IV substance dependence criteria | NSDUH questions | Total (%) | Adults (%) |
|---|---|---|---|
| 1. Spent a great deal of time over a period of a month getting, using, or getting over the effects of pain relievers (i.e. salience) | During the past 12 months, was there a month or more when you spent a lot of your time getting or using prescription pain relievers?<br>During the past 12 months, was there a month or more when you spent a lot of your time getting over the effects of the prescription pain relievers you used? | 13.48 | 12.99 |
| 2. Used pain relievers more often than intended or was unable to keep set limits on pain reliever use (i.e. difficulty keeping limits) | Were you able to keep to the limits you set, or did you often use prescription pain relievers more than you intended to? | 3.82 | 4.05 |
| 3. Needed to use pain relievers more than before to get desired effects or noticed that same amount of pain reliever use had less effect than before (i.e. tolerance) | During the past 12 months, did you need to use more prescription pain relievers than you used to in order to get the effect you wanted? | 17.32 | 17.27 |
| 4. Inability to cut down or stop using pain relievers every time tried or wanted to (i.e. unable to cut down) | During the past 12 months, were you able to cut down or stop using prescription pain relievers every time you wanted to or tried to? | 3.50 | 3.57 |
| 5. Continued to use pain relievers even though they were causing problems with emotions, nerves, mental health, or physical problems (i.e. use despite problems) | Did you continue to use prescription pain relievers even though you thought this was causing you to have problems with your emotions, nerves, or mental health?<br>Did you continue to use prescription pain relievers even though you thought this was causing you to have physical problems? | 5.42 | 5.52 |
| 6. Pain reliever use reduced or eliminated involvement or participation in important activities (i.e. activities given up or reduced) | During the past 12 months, did using prescription pain relievers cause you to give up or spend less time doing these types of important activities? | 5.34 | 5.15 |
| 7. Reported experiencing three or more pain reliever withdrawal symptoms at the same time that lasted longer than a day after pain reliever use was cut back or stopped. Symptoms include feeling kind of blue or down, vomiting or feeling nauseous, having cramps or muscle aches, having teary eyes or a runny nose, feeling sweaty, having enlarged pupils, or having body hair standing up on skin, having diarrhea, yawning, having a fever, having trouble sleeping (i.e. withdrawal) | During the past 12 months, did you have 3 or more of these symptoms at the same time that lasted for longer than a day after you cut back or stopped using prescription pain relievers? Feeling kind of blue or down, vomiting or feeling nauseous, having cramps or muscle aches, having teary eyes or a runny nose, feeling sweaty, having enlarged eye pupils, or having body hair standing up on your skin, having diarrhea, yawning, having a fever, having trouble sleeping. | 7.07 | 6.84 |



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are primarily of interest when conducting LCA: (1) the probability of being in each group (or latent class), which also provides estimates of the prevalence of latent class membership, and (2) conditional response probabilities or the probability that an individual in a given group (or latent class) will respond positively to a particular symptom. The two assumptions inherent to LCA that include local independence and non-differential measurement were met. The bivariate residuals (BVRs) conditional on class membership associated with each pair of dependence symptoms were examined. Each BVR is a measure of the overall association in the corresponding two-way contingency table (i.e. Pearson's Chi-square test statistic) divided by the degrees of freedom, given class membership; large BVRs indicate a violation of the local independence assumption. The conditional BVRs ranged 0.003–15.658 in the total sample, and 0.0005–12.355 in the adult sample. One approach for accounting for large BVRs between any two variables is to add a "direct effect" between the two variables to account for the residual correlation and improve overall model fit (Vermunt and Magidson, 2000). Including a direct effect between dependent symptoms with high BVR (e.g. difficulty cutting down and difficulty keeping limits) did not further improve our model fit or significantly change the estimates of the conditional probabilities. Gender as an active covariate was also included in the model to check for non-differential measurement; once again, the fit or probability profile of the groups (or latent classes) did not change and thus the assumption was also met. Furthermore, the latent class structure for the total sample and adults only was almost identical, presenting further evidence of non-differential measurement (Figure 1).

Individuals were then assigned to their most likely class (i.e. modal class) using posterior probabilities calculated from the conditional probabilities illustrated in Figure 1. It is worth noting that when cases are classified into classes or groups using the modal assignment, a certain amount of misclassification error is present (5.13% and 4.36% for the total and adult sample of past year opioid users, respectively). The expected sizes of the modal classes were thus only slightly different than those based on the estimated model.

All other analyses, including multinomial regression analyses were then carried out using STATA 9.0 (StataCorp, 2005); the latent classes estimated as per the modal assignment were regressed on a number of correlates, including socio-demographic (age, gender, race/ethnicity, income, education), subtypes of opioid analgesic users, and the SMI indicator among the adult opioid past year users only. Additional models were run controlling for past-year marijuana dependence. Finally, we examined the association between class membership and the DSM-IV defined diagnosis of opioid analgesic dependence (APA, 1994).

## Results

### *Description of the total sample of extramedical opioid analgesic users*

The four most common types of opioid analgesics used by past–year extramedical opioid analgesic users in the past year were: hydrocodone (66.5%, e.g. Vicodin®), propoxyphene (66.4%, e.g. Darvocet®), oxycodone (42.6%, e.g. Oxycontin®), and codeine (28.4%, e.g. Phenaphen with codeine®). Table 1 presents the weighted prevalence of each of the reported symptoms of extramedical opioid analgesic dependence. The most common symptoms in both the total and adult sample of past past-year opioid analgesic users were: tolerance (17.3% in each sample), salience (13.5% and 13.0%, respectively) and withdrawal (7.1% and 6.8%, respectively).

Overall, 8.3% of the past-year extramedical opioid analgesic users met DSM-IV criteria for past-year opioid analgesic dependence. Prevalence of dependence was highest in the APCH group (13.7%), followed by AP (10.7%), and lowest in Group A (5.5%, $p < 0.0001$).

The majority of the past-year opioid analgesic users had consumed alcohol (86.9%) in the past year, and a substantial percentage (52.6%) had tried marijuana once or more in the preceding year. Past-year use and DSM-IV defined dependence of alcohol and other substances among the total and the adult samples of past-year extramedical opioid analgesic users are presented in Tables 2 and 3.

### *Latent classes of past-year opioid analgesic users*

The best-fitting model in the total sample was the four-class model. Based on estimated probabilities, Class 1 included 83.76% of the past-year opioid analgesic users, and the probability of endorsing each of the seven symptoms of dependence for individuals in this class was very low (<0.001–0.05). Contrary to Class 1, individuals belonging to Class 4 (2.1% of all the past year users) had high probabilities of endorsing each of the seven symptoms of dependence (0.70–0.99). The



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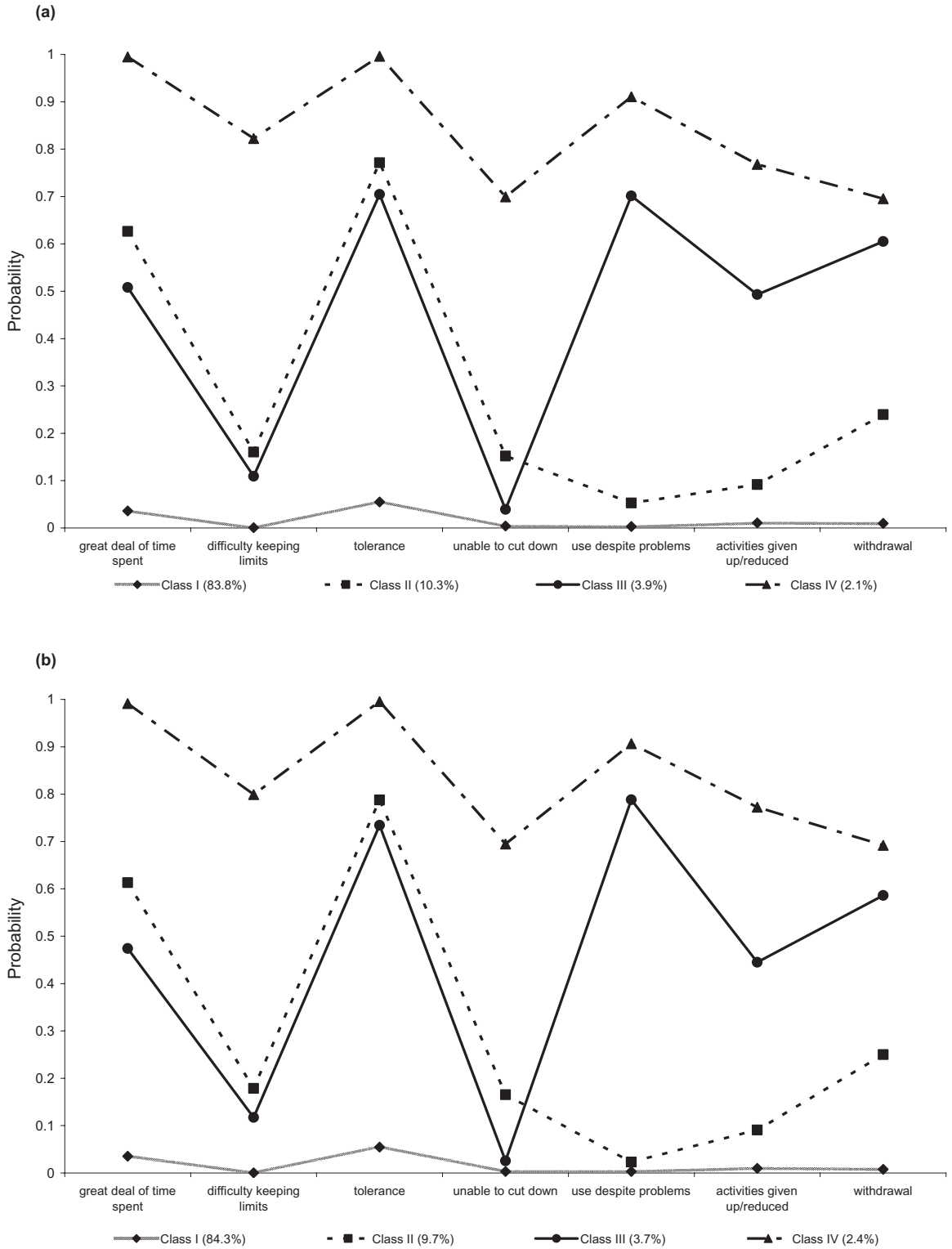


**Figure 1.** Weighted probability of endorsing dependence symptoms given latent class among all past year opioid analgesic users ($N$ = 7810, Figure 1a) and adult past year opioid analgesic users ($N$ = 5386, Figure 1b), NSDUH, 2002–2003.



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**Table 2.** Weighted prevalence of past year use and DSM-IV dependence on licit and illicit substances among all and adult past year extramedical opioid analgesic users, NSDUH, 2002–2003

| | All analgesic users *N* = 7810 | | Adult analgesic users *N* = 5386 | |
|---|---|---|---|---|
| | Past year use of substances | Past year dependence on substances | Past year use of substances | Past year dependence on substances |
| | *N* (%) | *N* (%) | *N* (%) | *N* (%) |
| Alcohol | 6896 (86.9) | 618 (15.3) | 4995 (88.7) | 466 (15.7) |
| Marijuana | 4830 (52.6) | 504 (9.1) | 3409 (51.8) | 306 (7.6) |
| Cocaine | 1826 (21.0) | 282 (3.5) | 1441 (22.0) | 235 (3.8) |
| Heroin | 160 (1.8) | 62 (1.0) | 117 (1.9) | 49 (1.2) |
| Hallucinogens | 1973 (17.5) | 63 (0.9) | 1364 (16.4) | 37 (0.7) |
| Inhalants | 881 (6.9) | 17 (0.2) | 416 (4.7) | 2 (0.02) |
| Any illicit | 7810 (100.0) | 853 (19.9) | 5386 (100.0) | 580 (19.3) |
| Stimulants | 1386 (13.9) | 153 (1.6) | 898 (12.8 | 97 (1.5) |
| Sedatives | 355 (4.9) | 54 (0.9) | 236 (4.9) | 33 (0.9) |
| Tranquilizers | 2172 (26.6) | 115 (1.6) | 1604 (27.0) | 75 (1.6) |

**Table 3.** Weighted prevalence of DSM-IV dependence on licit and illicit substances by latent class among all and adult past–year opiod users, NSDUH, 2002–2003

| | Class 1 *N* (%) | Class 2 *N* (%) | Class 3 *N* (%) | Class 4 *N* (%) |
|---|---|---|---|---|
| *All analgesic users* N = *7810* | | | | |
| Opioid analgesics* | 0 (0.0) | 226 (39.2) | 239 (84.6) | 133 (100.0) |
| Alcohol* | 472 (13.2) | 66 (19.8) | 59 (45.4) | 21 (28.6) |
| Marijuana* | 394 (8.5) | 54 (10.9) | 43 (18.4) | 13 (9.6) |
| Cocaine* | 182 (2.4) | 41 (6.8) | 34 (14.4) | 25 (15.7) |
| Heroin* | 30 (0.4) | 7 (0.5) | 16 (9.9) | 9 (12.4) |
| Hallucinogens* | 27 (0.4) | 14 (2.0) | 18 (6.0) | 4 (3.7) |
| Inhalants* | 7 (0.1) | 4 (0.5) | 5 (1.2) | 1 (0.3) |
| Any illicit* | 508 (11.7) | 158 (49.4) | 126 (91.3) | 61 (100.0) |
| Stimulants* | 65 (0.9) | 22 (1.8) | 40 (10.5) | 26 (12.4) |
| Sedatives* | 8 (0.1) | 12 (1.5) | 21 (13.1) | 13 (9.4) |
| Tranquilizers* | 21 (0.3) | 21 (1.7) | 47 (20.9) | 26 (21.7) |
| *Adult analgesic users* N = *5836* | | | | |
| Opioid analgesics* | 0 (0.0) | 164 (42.0) | 122 (84.3) | 107 (100.0) |
| Alcohol* | 365 (13.6) | 47 (20.3) | 36 (46.1) | 18 (28.6) |
| Marijuana | 247 (7.3) | 34 (9.3) | 18 (13.0) | 7 (7.5) |
| Cocaine* | 155 (2.6) | 34 (7.3) | 24 (16.9) | 22 (16.2) |
| Heroin* | 25 (0.5) | 5 (0.3) | 11 (12.3) | 8 (13.3) |
| Hallucinogens* | 19 (0.4) | 5 (1.2) | 11 (5.1) | 2 (3.0) |
| Inhalants | – | – | – | – |
| Any illicit* | 343 (10.8) | 112 (50.4) | 75 (90.2) | 50 (100.0) |
| Stimulants* | 48 (0.9) | 11 (1.3) | 18 (9.6) | 20 (11.1) |
| Sedatives* | 1 (0.0) | 7 (1.0) | 13 (16.0) | 9 (9.1) |
| Tranquilizers* | 13 (0.3) | 12 (1.3) | 26 (23.0) | 24 (23.2) |

* $p < 0.01$.



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probability profile of Classes 2 and 3 was similar for the following four symptoms, although slightly higher for Class 2: (1) salience (or spending a great deal of time getting/using substance or recovering from its effects); (2) use in larger amounts or for longer periods than intended; (3) tolerance; and (4) persistent desire/unsuccessful efforts to cut down/control use (Figure 1a). Although individuals in Class 3 had slightly lower probabilities of endorsing the aforementioned symptoms, they had a much higher probability of reporting withdrawal, continued use despite problems, and giving up or reducing important activities due to their use (Figure 1a). Thus, while differences between Classes 1 and 4 seem to be more quantitative in nature, Classes 2 and 3 differed qualitatively given the distinct pattern of symptoms endorsed by each group. The latent structure for the adult sample of past-year opioid analgesic users was almost identical (Figure 1b).

*Demographic profile of classes of past-year extramedical opioid analgesic users*

The demographic profile of the four latent class groups of all and adult opioid analgesic users is shown in Table 4. Males and females are almost equally represented across all groups, though Classes 2 and 4 had slightly more females than males. Whites were predominantly prevalent in all four groups. About 8% of Class 4 and 20% of Class 3 were adolescents (12–17 years old). Approximately two-thirds or more of the four classes included past-year users with a high school education or less. About 61% of Class 1 was characterized by opioid analgesics users only in the past year, compared to half as much (29%) in Class 4. About half of Class 4 belonged to Group APCH versus about 20% of Classes 1 and 2, and a third of Class 3. The same demographic trends were also observed among the adult past–year opioid users (Table 4). Additionally, close to 50% of Class 4 and Class 3 (49.8% and 46.8%, respectively) had a SMI score 13 and above (i.e. identified as having a possible serious mental illness) as compared to about 30% of Class 2 and 20% of Class 1 (Table 4).

*Latent class membership and users' characteristics*

Latent class regression models were used to test the associations between class membership and the demographic characteristics of the past-year opioid analgesic users, as well as their substance-using behaviors in the past year (Table 5). Female past-year opioid analgesic users were 1.5 and 2 times as likely to be in Classes 2 and 4 versus Class 1 (respectively). Young adolescent opioid analgesic users 12–17 years old (versus 18–25) were 1.5 times as likely to be in Class 3 (versus Class 1), and older age groups were more than three times as likely as 12–17 year olds to be in Class 4 (versus Class 1). African American past-year users were at higher odds of being in Class 2 versus Class 1. Respondents with a college level education were at a lower odds of being in Classes 3 and 2 (versus Class 1), compared to those with a high school level education or below. Respondents who reported an annual income between $20,000 and $75,000 had about two times or more the odds of being in Class 4 (versus Class 1) compared to those who reported an income of less than $20,000 (Table 5). Compared to past-year opioid analgesic users in Group A, those in Groups AP and APCH were at an increased odds of belonging to Classes 3 and 4 (versus Class 1), with stronger associations observed for the APCH group (Table 5). We then ran a separate model accounting for the past-year use of marijuana among the respondents; estimates of the odds ratios and their level of uncertainty were very slightly changed (results not shown, available upon request).

Overall, similar findings were observed among the adult sample as in the total sample by demographics (age, race, income and education). Unlike in the total sample, however, past-year use of substances (i.e. belonging to either Groups A, AP or APCH) did not statistically significantly differentiate opioid analgesic users in Class 2 from those in Class 1. Similarly, however, belonging to Groups AP and APCH was associated with an increased odds of being in Class 3 versus Class 1 [OR = 2.41 (1.26, 4.61) and 3.43 (1.79, 6.61), respectively], and those in Group APCH were five times as likely to be in Class 4 (versus Class 1) compared to those in Group A [OR = 5.36 (2.59, 11.1)]. Class membership was significantly related to the mental health of the adult past-year opioid analgesic users as measured by the SMI, an indicator of possible serious mental illness. Adult past-year opioid analgesic users who scored 13–24 (versus < 13) on the SMI (i.e. defined as possibly mentally ill) were 1.7 times as likely to be in Class 2 (95% CI = 1.20, 2.33), and about 3.5 times as likely to be in Classes 3 and 4 [OR = 3.49 (1.94, 6.29), and OR = 3.75 (1.96, 7.17), respectively]; these findings held true upon controlling for the respondents' use of marijuana in the preceding year (results not shown, available upon request).



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**Table 4.** Weighted prevalence of demographic characteristics, past–year drug use and mental health status by latent class among all and adult past–year opiod users, NSDUH, 2002–2003

| | Latent classes of past year extramedical opioid analgesic users | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | All opioid analgesic users (*N* = 7810) | | | | | | | | Adult opioid analgesic users (N = 5386) | | | | | | | |
| | Class 1 | | Class 2 | | Class 3 | | Class 4 | | Class 1 | | Class 2 | | Class 3 | | Class 4 | |
| | *N* | % | *N* | % | *N* | % | *N* | % | *N* | % | *N* | % | *N* | % | *N* | % |
| *Gender* | | | | | | | | | | | | | | | | |
| Males | 3540 | 54.0 | 313 | 44.2 | 122 | 51.5 | 57 | 43.8 | 2524 | 54.8 | 207 | 44.5 | 73 | 56.1 | 50 | 44.2 |
| Females | 3182 | 46.0 | 347 | 55.8 | 173 | 48.5 | 76 | 56.2 | 2171 | 45.3 | 220 | 55.5 | 84 | 43.9 | 57 | 55.8 |
| *Race* | | | | | | | | | | | | | | | | |
| White Non-Hispanics | 5031 | 72.7 | 474 | 66.0 | 229 | 80.4 | 113 | 88.2 | 3616 | 73.6 | 316 | 65.1 | 126 | 81.9 | 91 | 88.5 |
| African Americans | 522 | 8.33 | 64 | 14.4 | 22 | 7.3 | 5 | 3.9 | 317 | 7.7 | 36 | 15.0 | 13 | 6.5 | 4 | 4.3 |
| Hispanics | 796 | 14.7 | 85 | 15.1 | 23 | 9.4 | 7 | 5.4 | 512 | 14.2 | 49 | 15.2 | 10 | 10.0 | 6 | 4.6 |
| Others | 373 | 4.4 | 37 | 4.5 | 21 | 3.0 | 8 | 2.5 | 250 | 4.5 | 26 | 4.7 | 8 | 1.7 | 6 | 2.7 |
| *Age* | | | | | | | | | | | | | | | | |
| 12–17 years | 2027 | 15.4 | 247 | 19.2 | 123 | 19.8 | 27 | 8.4 | – | – | – | – | – | – | – | – |
| 18–25 years | 3525 | 33.3 | 304 | 31.6 | 131 | 28.9 | 60 | 26.1 | 3525 | 39.3 | 315 | 39.6 | 119 | 34.5 | 61 | 28.7 |
| 26–34 years | 558 | 20.1 | 52 | 19.9 | 15 | 10.5 | 21 | 25.1 | 558 | 23.8 | 53 | 24.2 | 14 | 13.5 | 21 | 27.3 |
| 35 years and older | 612 | 31.2 | 57 | 29.3 | 26 | 40.9 | 25 | 40.5 | 612 | 36.9 | 59 | 36.1 | 24 | 52.1 | 25 | 44.0 |
| *Education** | | | | | | | | | | | | | | | | |
| High school or less | 4701 | 60.3 | 519 | 69.7 | 235 | 71.4 | 88 | 66.7 | 2674 | 53.1 | 284 | 63.0 | 100 | 63.5 | 61 | 63.5 |
| Some college | 1448 | 25.3 | 111 | 25.2 | 51 | 25.1 | 31 | 20.7 | 1448 | 29.9 | 113 | 30.8 | 48 | 31.9 | 32 | 22.7 |
| College or more | 573 | 14.4 | 30 | 5.1 | 9 | 3.6 | 14 | 12.7 | 573 | 17.0 | 30 | 6.2 | 9 | 4.7 | 14 | 13.8 |


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**Table 4.** *Continued*

| | Latent classes of past year extramedical opioid analgesic users | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | All opioid analgesic users (*N* = 7810) | | | | | | | | Adult opioid analgesic users (N = 5386) | | | | | | | |
| | Class 1 | | Class 2 | | Class 3 | | Class 4 | | Class 1 | | Class 2 | | Class 3 | | Class 4 | |
| | *N* | % | *N* | % | *N* | % | *N* | % | *N* | % | *N* | % | *N* | % | *N* | % |
| *Income* | | | | | | | | | | | | | | | | |
| $ < 20,000 | 1901 | 25.6 | 189 | 26.2 | 97 | 28.9 | 28 | 14.7 | 1552 | 26.9 | 140 | 27.1 | 54 | 29.2 | 26 | 15.8 |
| 1$20,000–$49,999 | 2539 | 36.6 | 267 | 41.8 | 111 | 41.2 | 53 | 45.8 | 1742 | 36.1 | 159 | 41.2 | 65 | 44.1 | 47 | 47.3 |
| $50,000–$74,999 | 1035 | 18.2 | 103 | 14.9 | 44 | 11.4 | 30 | 25.1 | 642 | 18.1 | 63 | 14.9 | 16 | 8.5 | 20 | 23.7 |
| $75,000 or more | 1247 | 19.7 | 101 | 17.2 | 43 | 18.5 | 22 | 14.3 | 759 | 18.9 | 65 | 16.8 | 22 | 18.3 | 14 | 13.2 |
| *Past year analgesic groups* | | | | | | | | | | | | | | | | |
| Opioid analgesics only (Group A) | 3842 | 60.5 | 269 | 52.5 | 105 | 36.3 | 25 | 28.6 | 2542 | 59.9 | 180 | 55.9 | 51 | 34.0 | 24 | 30.9 |
| Opioid analgesics & prescription drugs only (Group AP) | 1383 | 19.5 | 198 | 25.4 | 90 | 28.1 | 38 | 24.7 | 945 | 19.0 | 113 | 22.5 | 44 | 27.8 | 27 | 23.5 |
| Opioid analgesics & prescription drugs & cocaine/heroin (Group APCH) | 1497 | 20.0 | 193 | 22.1 | 100 | 35.6 | 70 | 46.7 | 1208 | 21.1 | 134 | 21.6 | 62 | 38.2 | 56 | 45.6 |
| *SMI* | | | | | | | | | | | | | | | | |
| <13 | – | – | – | – | – | – | – | – | 3704 | 80.6 | 263 | 69.6 | 70 | 53.2 | 45 | 50.2 |
| 13–24 | – | – | – | – | – | – | – | – | 991 | 19.4 | 164 | 30.5 | 87 | 46.8 | 62 | 49.8 |

*$p < 0.02$.

–, data available for adults aged 18 years or older only.

**Table 5.** Adjusted (unadjusted) odds ratio estimates and 95% confidence intervals for class membership and selected characteristics of all past-year opioid analgesic users ($N = 7810$), NSDUH, 2002–2003

| Variables in the model | Latent classes of past year extramedical opioid analgesic users | | | | | |
|---|---|---|---|---|---|---|
| | Class 2 | | Class 3 | | Class 4 | |
| | A-OR (UA-OR) | 95% CI (95% CI) | A-OR (UA-OR) | 95% CI (95% CI) | A-OR (UA-OR) | 95% CI (95% CI) |
| *Gender* | | | | | | |
| Males | 1.00 | – | 1.00 | – | 1.00 | – |
| Females | 1.51 (1.48) | 1.14, 2.02 (1.12, 1.97) | 1.18 (1.10) | 0.75, 1.85 (0.67, 1.81) | 2.02 (1.50) | 1.18, 3.43 (0.88, 2.59) |
| *Race* | | | | | | |
| White Non-Hispanics | 1.00 | – | 1.00 | – | 1.00 | – |
| African Americans | 1.95 (1.92) | 1.15, 3.31 (1.14, 3.24) | 0.85 (0.79) | 0.43, 1.67 (0.42, 1.51) | 0.49 (0.39) | 0.14, 1.78 (0.12, 1.27) |
| Hispanics | 1.14 (1.13) | 0.74, 1.76 (0.73, 1.74) | 0.61 (0.58) | 0.25, 1.49 (0.24, 1.39) | 0.40 (0.31) | 0.14, 1.16 (0.12, 0.81) |
| Others | 1.14 (1.13) | 0.59, 2.20 (0.59, 2.17) | 0.65 (0.60) | 0.32, 1.31 (0.30, 1.23) | 0.54 (0.46) | 0.18, 1.63 (0.15, 1.39) |
| *Age* | | | | | | |
| 12–17 years | 1.00 | – | 1.00 | – | 1.00 | – |
| 18–25 years | 0.89 (0.76) | 0.68, 1.16 (0.61, 0.96) | 0.64 (0.68) | 0.43, 0.94 (0.50, 0.91) | 1.64 (1.45) | 0.85, 3.17 (0.78, 2.68) |
| 26–34 years | 1.09 (0.80) | 0.72, 1.65 (0.54, 1.17) | 0.52 (0.41) | 0.26, 1.06 (0.21, 0.78) | 3.24 (2.30) | 1.52, 6.89 (1.15, 4.62) |
| 35 years and older | 0.95 (0.75) | 0.62, 1.45 (0.51, 1.12) | 1.32 (1.02) | 0.68, 2.59 (0.55, 1.91) | 3.58 (2.39) | 1.47, 8.71 (1.05, 5.43) |
| *Education* | | | | | | |
| High school or less | 1.00 | – | 1.00 | – | 1.00 | – |
| Some college | 0.87 (0.86) | 0.63, 1.22 (0.63, 1.18) | 0.87 (0.84) | 0.45, 1.66 (0.46, 1.52) | 0.56 (0.74) | 0.30, 1.05 (0.40, 1.35) |
| College or more | 0.32 (0.31) | 0.17, 0.60 (0.17, 0.56) | 0.21 (0.21) | 0.08, 0.58 (0.08, 0.53) | 0.54 (0.80) | 0.21, 1.36 (0.34, 1.85) |
| *Income* | | | | | | |
| <$20,000 | 1.00 | – | 1.00 | – | 1.00 | – |
| $20,000–$49,999 | 1.19 (1.11) | 0.84, 1.69 (0.79, 1.58) | 0.98 (1.00) | 0.58, 1.64 (0.58, 1.71) | 2.26 (2.17) | 1.08, 4.74 (1.03, 4.57) |
| $50,000–$74,999 | 0.94 (0.80) | 0.61, 1.44 (0.52, 1.22) | 0.59 (0.55) | 0.32, 1.10 (0.30, 1.02) | 2.76 (2.40) | 1.32, 5.78 (1.19, 4.84) |
| $75,000 or more | 1.15 (0.85) | 0.74, 1.78 (0.55, 1.34) | 0.93 (0.83) | 0.48, 1.78 (0.42, 1.64) | 1.56 (1.27) | 0.72, 3.36 (0.58, 2.75) |
| *Past-year analgesic groups* | | | | | | |
| Opioid analgesics only (Group A) | 1.00 | – | 1.00 | – | 1.00 | – |
| Opioid analgesics & prescription drugs only (Group AP) | 1.65 (1.51) | 1.22, 2.23 (1.11, 2.05) | 2.22 (2.41) | 1.35, 3.67 (1.44, 4.04) | 2.59 (2.70) | 1.04, 6.41 (1.10, 6.58) |
| Opioid analgesics & prescription drugs & cocaine/heroin (Group APCH) | 1.49 (1.27) | 1.09, 2.03 (0.92, 1.76) | 3.21 (2.97) | 1.89, 5.43 (1.77, 4.97) | 6.15 (4.95) | 2.97, 12.72 (2.19, 11.16) |

*Note:* Class 1 is the reference class; A-OR, adjusted odds ratios, controlling for all variables in the model; UA-OR, unadjusted odds ratios; CI, confidence interval.



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*Latent class membership and DSM-IV defined abuse and dependence*

Overall, 8.3% of the past-year extramedical opioid analgesic users were diagnosed with DSM-IV defined opioid analgesic dependence in the year preceding assessment. No one in Class 1 was diagnosed with DSM-IV opioid analgesic dependence in the preceding year, compared to 39.2% of those in Class 2, 84.6% of those in Class 3, and 100% of individuals in Class 4 ($p < 0.0001$). Similar trends were observed among the adult past-year opioid analgesic users (0%, 42% 84.3%, and 100%, respectively, $p < 0.0001$).

Among the total sample of past-year opioid analgesic users, 4.2% of those in Class 1, 13.0% of Class 2, 5.8% of Class 3, and 0% of Class 4 met DSM-IV criteria for abuse ($p < 0.001$). A similar pattern was found among the adult opioid analgesic users: 4.2%, 11.7%, 5.6%, and 0%, respectively ($p < 0.001$). It is worth noting that as per DSM-IV criteria, respondents should not meet the criteria for dependence for the same class of substance to be diagnosed with substance abuse.

## Discussion

Despite the growing concern regarding opioid analgesic use and dependence in the US, there is a paucity of available studies investigating problems of dependence linked to extramedical use of opioid analgesics in the general population (Huang et al., 2006; Martins et al., 2007). Findings from this study fill this gap, identifying distinct subgroups of extramedical opioid analgesic users given the probability of their response patterns to the DSM-IV clinical features or dependence symptoms related to this class of drugs.

This study's findings have several implications for nosological research, as well as tertiary prevention and treatment. Based on the best-fitting LCA model, four mutually exclusive groups of extramedical past year opioid analgesic users were identified. The vast majority of users (84%) belong to a class (Class 1) characterized by low probability of dependence symptoms. No members of this class met criteria for DSM-IV drug dependence. Two classes (Class 2 and Class 3) both shared similarly high probability of symptoms of salience and tolerance and low probability of difficulty keeping limits and cutting down, but differed with respect to symptoms of withdrawal, use despite problems and giving up important activities. Class 2 accounted for 10% of extramedical opioid analgesic users and had low probability of other dependence symptoms, and approximately one-third (39%) of the respondents assigned to this class met DSM-IV criteria for dependence. In contrast, 85% of those in Class 3 met criteria for dependence and this class accounted for 4% of opioid users. The final class, accounting for the remaining 2% of extramedical analgesic opioid users, was characterized by high probability of all dependence symptoms. All members of this class met criteria for dependence. These results indicate significant heterogeneity among those identified as cases of DSM-IV dependence for opioid analgesics. Further results from latent class regression models indicate that associations with demographic, drug use, and psychiatric disorder characteristics differ across the four classes.

While it may seem that those diagnosed as being dependent on opioid analgesics according to DSM-IV criteria have been split into Classes 3 and 4, important distinctions can be made. Close to two-thirds of those in Class 2, marked by a somewhat high probability of reporting salience and tolerance, and about a 10% chance of reporting difficulty keeping limits and/or cutting down, were not identified by DSM-IV classification. Moreover, 19% of past-year opioid analgesic users (who were in Class 3, characterized by a great number of clinical dependence features), were identified as non-dependent according to DSM-IV classification. Thus, despite their similarity, identifying individuals based on the number of symptoms endorsed, rather than the pattern of symptoms reported, may be portraying the picture only partially.

Moreover, while the prevalence of DSM-IV defined opioid analgesic dependence consistently increased across Class 1 through Class 4, suggesting that these classes varied along a continuum of severity, important qualitative differences were noted between the classes. Respondents in Class 3 (the more "severe" class) had somewhat similar probability of reporting salience, tolerance, difficulty keeping limits, and inability to cut down as those in Class 2 (slightly higher for those in Class 2), but a much higher probability of continued use despite problems, activities given up/reduced and withdrawal.

Given that the probability of reporting "having problem keeping limits" and "difficulty cutting down" by opioid analgesic users in Class 3 is low, and the probability of endorsing all other clinical features of dependence is relatively high, one could construe that past-year opioid analgesic users in Class 3 may "believe" they have their use under control or may not wish to



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reduce their use. We thus expect that such users will be the ones most likely to be classified clinically as being dependent, and indeed five out of six of those in Class 3 met DSM-IV criteria for dependence, compared to only a third of those in Class 2. Differences between individuals in Classes 2 and 3 should be further interpreted in light of other findings from this study which show that adolescents (12–17 year olds) are more likely than adults aged 18–34 to be in Class 3 versus Class 1, suggesting this group of users is most likely a young group of individuals who may think they have their use under control, when clearly it is not.

Opioid analgesic users in Class 2 reported spending a great deal of time getting or using the opioid analgesics and have developed tolerance, but they reported no additional problems. Thus, whether this group is on the verge of developing or has already developed dependence is uncertain. This group is less likely be detected epidemiologically using DSM-IV criteria, and is probably also less likely to seek professional help for substance use or for dealing with problems of salience and tolerance before they develop a "full-blown" opioid analgesic dependence syndrome. Future longitudinal research using latent transition models will help shed light on whether Class 2 is a transitional state, especially for younger opioid analgesic users, who might move on to Class 3 in later years. Adults with serious mental health problems were also more likely to be in Class 2 versus Class 1 as compared to those with no mental health problems, suggesting that people with mental health problems are also part of this potentially undetected yet "at-risk" group. One should keep in mind that our sample is comprised of "extramedical" opioid analgesic users, which stresses even more the need to identify and pay special attention to this group of users, and encourage them to recognize their problem, and to seek treatment. Adults with serious mental health problems were also increasingly more likely to be in Classes 3 and 4, corroborating other findings linking opioid analgesic misuse and psychiatric comorbidity (Dowling et al., 2006; Huang et al., 2006; Romach et al., 1999).

The fact that very few published studies have examined opioid analgesic dependence or symptoms of dependence in the general population in the US limits our efforts to compare our findings with the work of others. Most recently however, a study by Huang et al. (2006) found that males, Blacks (versus Whites), and 18–29 year olds (versus 30–44 year olds) are at higher odds of opioid analgesic abuse/dependence. Another study by Simoni-Wastila et al. (2004) investigated problem use of narcotic analgesics, defined as meeting two of five dependence criteria, and found that being female, unmarried, and 12–17 years old (versus 18–24 years old) to increase the odds of narcotic analgesics problem use. Similar to the work of Simon-Wastila et al. (2004), but unlike that of Huang et al. (2006), we found females to be at higher odds of being in Class 2 and Class 4 (though of equal odds as males to be in Class 3). Young adolescents aged 12–17 (versus 18–25) were at a higher odds of being in Class 3; older age groups were more likely to be in Class 4 (versus Class 1). With respect to race/ethnicity, we found no differences, except for Class 2, whereby African Americans were twice as likely as Whites to be in that class.

Our findings should be interpreted in light of several limitations, mainly inherent to data unavailable in the NSDUH. One is that it is not possible to distinguish whether these extramedical opioid analgesic users first started using these drugs because they were legitimately prescribed for them or if they initiated opioid analgesic use illegally. This is important when trying to understand the natural history of the use of these substances, as well as the profile of these users, which may be distinct. However, the fact that close to 25% (1860 of the total 7810) of extramedical past-year opioid analgesic users in our study have also used heroin/cocaine in the same year, suggests that some of the individuals currently misusing opioid analgesics may be indeed obtaining them illegally.

Another limitation may be misclassification. Although past-year dependence questions for the different drug classes are asked separately in the NSDUH, there might be some misclassification among respondents who are past-year users of more than one class of drugs (e.g. respondents who are past-year analgesic and cocaine users might attribute cocaine dependence symptoms to the analgesic they use and vice-versa). Moreover, the NSDUH does not assess the exact amount of opioid analgesics an individual took each time s/he used the substance in the preceding year.

Notwithstanding these limitations, the NSDUH is a large dataset using an epidemiologically-sound survey design to assess a nationally representative sample of individuals aged 12 years or older, which has allowed us to employ such complex statistical methods as LCA,



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and to generalize our results to past-year extramedical opioid analgesic users in the US population at risk of experiencing dependence symptoms or developing dependence. Moreover, the ongoing debate regarding the utility of a categorical versus a dimensional approach for classifying substance user disorders not only highlights the utility of this study's findings but also stresses its timeliness. In a recent review article, Helzer et al. (2006) concluded that the DSM-V may benefit from including both categorical and dimensional classifications but that "any dimensional approach be linked to the categorical definition", which is the approach adopted in this paper.

Several important research questions remain to be addressed. Latent class models could be extended to test for differences in classification between recent-onset users and persistent users, as well as extramedical opioid analgesic users versus opioid users who legitimately use these substances as prescribed for them (data not available in NSDUH). Latent transition analysis (LTA) using longitudinal data may also help increase our understanding with respect to the probability of transitioning from a class at one point in time to another class at a later time point (Muthén and Muthén, 2000). Moreover, this study needs to be replicated in different samples (i.e. clinical populations) before any definite conclusions can be confidently made.

Results from this study provide an initial glimpse into the heterogeneity of response to extramedical use of opioid analgesics, which has important implications for the diagnosis of opioid analgesic dependence, as well as prevention and management. This study is unique, and the first to our knowledge to empirically identify latent classes of extramedical opioid analgesic users based on the probability of the occurrence of possible patterns of symptoms of opioid dependence among a sample from the general population. The use of latent class models can shed light on the classification and distribution of extramedical opioid analgesic dependence symptoms in the US general population, and identification of subgroups that vary with respect to their potential need for treatment and stage of progression to problematic involvement with this class of drugs.

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**Declaration of Interests**

The authors have no competing interests.

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